

REMARKS

Reconsideration of the pending claims is urged in light of the comments below and attached Declaration of Mr. Kaasgaard. New claims 32 and 33 are added. No new matter is added.

It is respectfully submitted that the arguments herein place this case in condition for allowance. Reconsideration of the application is urged.

I. The Rejection of Claims 14-23, 25, 26, 29 and 30 under 35 U.S.C. 102(e)

Claims 14-23, 25, 26, 29 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by Kaasgaard et al., U.S. patent publication no. 2004/0175812 (hereinafter simply referred to as "Kaasgaard"). The Examiner alleges that Kaasgaard discloses adding the polyol or carbohydrates disclosed therein "prior to" recovery, thus during fermentation. Applicants respectfully traverse this rejection.

Kaasgaard does not anticipate the claimed invention. Claim 14 requires, among other things, adding one or more listed compounds to the culture medium before and/or during fermentation. As explained in the specification, carbohydrate and/or polyol are added to the culture medium, wherein the microorganism is not, or only to a low extent able to metabolize them. See e.g., Summary on page 2. Accordingly, Applicants have discovered that the specified compounds are suitable for use during fermentation. Conversely, Kaasgaard is directed towards a method for recovering a protein of interest from a culture solution by adding a polyol, and/or a carbohydrate, and/or a derivative thereof, to the culture solution during recovery processing. See, e.g., paragraph 9 of Kaasgaard, which describes added certain compounds to the culture solution prior to, or immediately after, said recovery step. Further, paragraph 12 describes, *inter alia*, avoiding formation of protein crystals/precipitates during recovery processing. Moreover, nowhere does Kaasgaard, including paragraphs 0007-0009, 0051-0057, 0080-0096 describe anything other than adding the compounds prior to a recovery step. Nowhere does Kaasgaard describe adding one or more of the compounds to the culture medium before and/or during fermentation, as required by the instant claims.

With respect to the "prior to" language cited by the Examiner, Applicants note Kaasgaard teaches nothing more than adding prior to a recovery step. Such steps are set forth for example in paragraphs [0045], [0046], [0047], [0048], [0049] and [0050]. Attached hereto is a declaration of Sven Kaasgaard and inventor in the present case

and the Kaasgaard reference. Mr. Kaasgaard explains that one would not infer from the Kaasgaard reference that adding the polyols and/or carbohydrates disclosed in Kaasgaard prior to a recovery step would mean adding the compounds during fermentation. Rather Kaasgaard is limited to adding the polyols and/or carbohydrates prior to the specified recovery steps. See for paragraph 5 of the attached Kaasgaard declaration. In other words, each of the specified recovery steps occurs after fermentation. Applicants believe that if one were to review the reference as a whole, there is no indication that any of polyols and/or carbohydrates of Kaasgaard should be added before and/or during fermentation. Accordingly, Kaasgaard does not anticipate the claimed invention and reconsideration is urged.

Anticipation requires enablement. To anticipate, the identical subject matter must not only be previously known, but the knowledge must be sufficiently enabling to place the information in the possession of the public. See *Seymour v. Osborne*, 78 U.S. 516 (1870). Kaasgard is deficient in that it fails to indicate which polyols and/or carbohydrates of Kaasgaard may be added before or during fermentation. Kaasgard is devoid of any instruction as to the possible choices of polyols and/or carbohydrates that may be suitable for a fermentation medium, thus could not enable the claimed invention solely on the use of the alleged "prior to" language. The present invention is based on an understanding that the polyol and carbohydrate selected include compounds which are not, or only to a low extent, capable of being metabolized by the fermentation microorganisms. Without this understanding, one of ordinary skill in the art would not simply add the polyol and carbohydrate to the fermentation step. Indeed, Mr. Kaasgaard in his attached declaration states "One of skill in the art would not consider adding any of the polyols and/or carbohydrates such as those described in U.S. Publication No. 2004/0175812 during fermentation, as it most often would affect the growth of the microorganisms and the production of the enzyme product negatively. The present invention overcomes this because the polyol and carbohydrate are selected to include only compounds which are not, or only to a low extent, capable of being metabolized by the fermentation microorganisms."

As Kaasgard does not describe adding the compounds of claim 14 during fermentation, but rather just before and/or during a recovery step, the public was not in possession of the benefits of applying the compounds in a fermentation step.

Accordingly, Kaasgard is not an enabling reference suitable for use in an anticipation rejection and the reference does not anticipate the claimed invention. Reconsideration is urged.

II. The Rejection of Claims 14-31 under 35 U.S.C. 103(a)

Claims are rejected under 35 U.S.C. 103 as obvious over Kaasgaard. This rejection is respectfully traversed.

As explained above, Kaasgaard is deficient in that it does not describe, adding 1,2-propandiol, 1,3-propandiol, ethylene glycol, trehalose, xylitol, arabitol, dulcitol, erythritol, sorbitol and a polyether having an average molecular weight less than 1000 to the culture medium before and/or during fermentation. Specifically, nowhere does Kaasgaard describe adding the specified compounds before or during fermentation. In other words, Kaasgaard is limited to adding the polyols and carbohydrates of Kaasgaard prior to, or during a recovery step. Mr. Kaasgaard himself, an inventor in the present disclosure and the Kaasgaard reference explains in the attached declaration:

In my opinion, one of skill in the art would not infer from U.S. Publication No. 2004/0175812 that adding the polyols and/or carbohydrates disclosed therein prior to a recovery step would mean adding the compounds during fermentation. Rather, U.S. Publication No. 2004/0175812 is limited to adding the polyols and carbohydrates disclosed therein prior to the specified recovery steps such as those identified in paragraphs [0045], [0046], [0047], [0048], [0049] and [0050]. Each of these recovery steps occur after fermentation.

As Kaasgaard fails to teach each and every element, Kaasgaard alone, does not make the claimed invention obvious.

Moreover, one of ordinary skill in the art would not consider adding the compounds specified in claim 14 to the fermentation step based on the Kaasgaard reference. As explained in the attached declaration of Mr. Kaasgaard:

One of skill in the art would not consider adding any of the polyols and/or carbohydrates described in U.S. Publication No. 2004/0175812 during fermentation, as it most often would affect the growth of the microorganisms and the production of the enzyme product negatively. The present invention overcomes this because the polyol and carbohydrate are selected to include only compounds which are not, or only to a low extent, capable of being metabolized by the bacterial fermentation microorganisms.

Accordingly, nothing in the Kaasgaard reference would direct one of ordinary skill in the art to select the specified compounds in claim 14, those compounds which are not, or less likely to be metabolized by the fermentation medium. Kaasgaard does not make the claimed invention obvious. Reconsideration is urged.

III. The Rejection of Claims 14-31 under 35 U.S.C. 103(a)

Claims 14-31 are rejected under 35 U.S.C. 103 as obvious over Brothers *et al.* (U.S. 4,673,647) in view of Schreiber (U.S. 4,016,039) and GB 1001173 and Boyer *et al.* (5,385,837). This rejection is respectfully traversed.

Brothers *et al.* is deficient and it does not disclose the process of the present disclosure. Specifically, Brothers does not teach adding one or more of the recited compounds to the culture medium before and/or during fermentation. For example, see Column 3, lines 15-40. Here, Brothers explains that in Step 1 the culture is of enzyme secreting microorganism grown in a fermentor. Then, the fermentation products are moved to a drop tank (Step 2). One of ordinary skill in the art would understand that Step 2, begins the recovery process. In other words, the polyol solvent added in Step 6, does not take place during fermentation.

Further, one of ordinary skill in the art would not necessarily realize that such polyols would be successful during the fermentation step. More specifically, one of skill in the art would not consider adding any of the polyols and/or carbohydrates during fermentation, as it may affect the growth of the microorganisms and the production of the enzyme product negatively. While not wishing to be bound by the present disclosure, or statements, it is believed the present disclosure works with the selected compounds because the claimed compounds include only compounds which are not, or only to a low extent, capable of being metabolized by the fermentation microorganisms.

Accordingly, Brothers is deficient in providing instruction on applying the claimed compounds before and/or during fermentation.

Schreiber fails to cure the deficiencies of Brothers. Specifically, Schreiber discloses a process for recovery of proteins involving adding polyoxyethylene glycol after fermentation. See for example the preamble of claim 1 which states "in the process of recovering an alkaline protease from the fermentation of *Bacillus licheniformis* in aqueous solutions". See also, Example 1, which states "A fermentor broth . . . was liberated of

cell residues and concentrated . . ." Thus, PEG was added to the concentrate, i.e., during recovery and after fermentation.

GB 1001173 is deficient and fails to cure the deficiencies of Brothers and Schreiber. Specifically, GB 1001173 is directed to a process of production of a galactose oxidase from a fungus (*Polyporus circinatus Fr.*). The instant claims relate to bacterium. The reference provides no guidance on bacterial fermentation, thus does not show adding the specified compounds during the requisite fermentation.

Boyer et al. is directed to production of an alkaline *Bacillus* protease, in which suitable carbon sources are indicated as glucose, mannose, fructose, mannitol, maltose, cellobiose, sucrose, dextrin, starch, hydrolyzed starch, molasses, etc.

None of the cited reference teach or suggest, alone or in combination, adding 1,2-propandiol, 1,3-propandiol, ethylene glycol, trehalose, xylitol, arabitol, dulcitol, erythritol, sorbitol and a polyether having an average molecular weight less than 1000 to a bacterial culture medium before and/or during fermentation in accordance with the claimed process.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV: New claims

New claims 32 and 33 are added. The USPTO is authorized to charge the deposit account of Novozymes North America, Inc, 50-1701 should any additional fees be due.

V. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: April 30, 2008

/Michael W. Krenicky Reg # 45411/
Michael W. Krenicky Reg. # 45,411
Novozymes North America, Inc.
500 Fifth Avenue, Suite 1600
New York, NY 10110
(212)840-0097